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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/382,622	08/25/1999	H. CRAIG DEES	PHO-107-DIV	5477

7590 04/11/2006
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EXAMINER	
GABEL, GAILENE	
ART UNIT	PAPER NUMBER

1641

DATE MAILED: 04/11/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No. 09/382,622	Applicant(s) DEES ET AL.	
	Examiner Gailene R. Gabel	Art Unit 1641	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).

Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1) ☒ Responsive to communication(s) filed on 09 January 2006.

2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.

3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4) ☒ Claim(s) 1,4,10,14,15,51,52,55-57,61,65,66 and 68 is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5) ☒ Claim(s) 68 is/are allowed.

6) ☒ Claim(s) 1,4,10,15,51,52,55-57,61,65 and 66 is/are rejected.

7) ☒ Claim(s) 14 is/are objected to.

8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9) ☐ The specification is objected to by the Examiner.

10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a) ☐ All b) ☐ Some * c) ☐ None of:

1. ☐ Certified copies of the priority documents have been received.

2. ☐ Certified copies of the priority documents have been received in Application No. _____.

3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) <input type="checkbox"/> Notice of References Cited (PTO-892) 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.	4) <input type="checkbox"/> Interview Summary (PTO-413) Paper No(s)/Mail Date. _____. 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152) 6) <input type="checkbox"/> Other: _____.
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DETAILED ACTION

Amendment Entry

1. Applicant's amendment and response filed January 9, 2006 is acknowledged and has been entered. Claims 1, 10, and 51 have been amended. Accordingly, claims 1, 4, 10, 14, 15, 51, 52, 55-57, 61, 65, 66, and 68 are pending and are under examination.

Moot or Withdrawn Rejections

2. Rejections not reiterated herein have been withdrawn.

3. In light of Applicant's amendment, the rejection of claims 1, 4, 10, 14, 15, 51, 52, 55-57, 61, 65, and 66 under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement, is hereby, withdrawn.

4. Upon further consideration, the statutory double patenting rejection of claims 1, 4, 10, 15, 51, 52, 55-57, 61, 65, and 66 under 35 U.S.C. 101 as claiming the same invention as that of claims 1, 4, 6, 7, 26, 29, 31, 32, 42, 43, and 45-48 of copending ASN 09/799,785 in light of Wihdholz et al. (Merck Index (1983) published by Merck Co.), is being withdrawn.

5. In light of Applicant's submission of a Terminal Disclaimer, the rejection of claims 1, 4, 10, 15, 51, 52, 55-57, 61, 65, and 66 under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1, 4-6, 12-14, 29,

Art Unit: 1641

32-34, 39, 40, and 46-49 of copending Application No. 09/817,448 in view of Heitz et al. (US Patent 4,846,789), is hereby, withdrawn.

New Grounds of Rejection

Obviousness Double Patenting

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and, *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

6. Claims 1, 4, 10, 15, 51, 52, 55-57, 61, 65, and 66 are provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1, 4, 6, 7, 26, 29, 31, 32, 42, 43, and 45-48 of copending ASN 09/799,785 in view of Wihdholz et al. (Merck Index (1983) published by Merck Co.).

Although the conflicting claims are not identical, they are not patentably distinct from each other because the conflicting claims are drawn to a radiosensitizer agent for treatment of cancer tissue and tumors comprising of a halogenated xanthene which interacts with applied ionizing radiation to enhance therapeutic efficacy of the ionizing radiation.

Art Unit: 1641

ASN 09/799,785 differs from the claimed invention in reciting that the medicament which is a radiosensitizer agent consists of "an aqueous solution of sodium, potassium, and lithium salt of a halogenated xanthene".

Windholz et al., however, specifically provide that halogenated xanthenes such as 4,5,6,7 tetrabromoerythrosin or Rose Bengal are known to be derivatized so as to contain sodium, potassium, and lithium salts as derivatives. Accordingly, this is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

Maintained Rejections

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless --

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

7. Claims 1, 10, 51, 52, 56, 57, and 66 are rejected under 35 U.S.C. 102(b) as being anticipated by Heitz et al. (US Patent 4,846,789).

Heitz et al. disclose halogenated xanthene dyes, which are administered to warm blooded animals and incorporated into infected tissue for activation by electromagnetic radiation (see Abstract and Figure 5). According to Heitz et al., the halogenated xanthene dyes may absorb radiation at wavelengths outside of the visible spectrum including near infrared, and near to far ultraviolet spectrum (see column 3, lines 40-44).

Art Unit: 1641

Heitz et al. teach that fluorescein derivatives having one or more substituents in the 4, 5, 6, 7, 2', 4', 5', and 7' positions selected from the group consisting of F, Cl, Br, with xanthene dyes including erythrosin B, phloxin B, eosin, and Rose Bengal are especially important (see column 4, lines 12-31). These halogenated xanthene dyes are incorporated into pharmaceutical delivery vehicles such as capsules, pellets, or salt blocks for oral administration.

With respect to the recitation of "an aqueous solution of a halogenated xanthene" the solubility property of compounds such as 4,5,6,7-tetrabromoerythrosin when solubilized by aqueous solution into liquid phase, i.e. *highly soluble in aqueous solution, demonstrate a preference for selective partitioning into hydrophobic environments, such as within cell membranes*, is an inherent property which does not change the structural composition of the claimed product. The discovery of a new property of an otherwise known compound or product such as 4,5,6,7-tetrabromoerythrosin, discovered to be highly soluble with demonstrated characteristic preference for selective partitioning into hydrophobic environments and which is capable of enhancing efficacy of ionizing radiation applied to cancer or tumor in radiation therapy, does not render the product novel, unless otherwise, rendered novel or nonobvious from a modification or variation of its original chemical structure, i.e. "derivatized 4,5,6,7-tetrabromoerythrosin by attachment to a biological targeting moiety", that is structurally different, novel, and nonobvious from all other commercially known halogenated xanthenes.

With respect to the recitation of "activated using X-rays having an energy greater than 30 keV" in claim 10, "using radiosensitization or ionizing radiation, ...

approximately greater than or equal to 1 keV and less than or equal to approximately 1000 MeV” in claims 51 and 52, “[interacting with ionizing radiation applied... which] comprises X-rays” in claim 56, and “X-rays have an energy between 30 kiloelectron volts and 1000 megaelectron volts” in claim 57, a recitation of the intended use of the claimed invention must result in a structural difference between the claimed invention and the prior art in order to patentably distinguish the claimed invention from the prior art. If the prior art structure is capable of performing the intended use, then it meets the claim. See *In re Casey*, 370 F.2d 576, 152 USPQ 235 (CCPA 1967) and *In re Otto*, 312 F.2d 937, 939, 136 USPQ 458, 459 (CCPA 1963).

With respect to halogenated xanthenes such as 4,5,6,7-tetrabromoerythrosin being an imaging contrast agent, the discovery of a new property of an otherwise known compound or product such as 4,5,6,7-tetrabromoerythrosin, discovered to characteristically exist as an imaging contrast agent which is capable of enhancing efficacy of ionizing radiation applied to cancer or tumor in radiation therapy, does not render the product novel, unless otherwise, rendered novel or nonobvious from a modification or variation of its original structure, i.e. “derivatized 4,5,6,7-tetrabromoerythrosin by attachment to a biological targeting moiety”, that is structurally different, novel, and nonobvious from all other commercially known halogenated xanthenes.

Claim Rejections - 35 USC § 103

Art Unit: 1641

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

8. Claims 4, 15, 55, 61, and 65 are rejected under 35 U.S.C. 103(a) as being unpatentable over Heitz et al. (US Patent 4,846,789) in view of Williams et al. (US 5,576,013).

Heitz et al. has been discussed supra. Heitz et al. differ from the instant invention in failing to teach that the halogenated xanthene includes as a functional derivative, at least one targeting moiety such as those recited in claims 4, 15, 55, 61, and 65, i.e. chelators, complexing agents, polyacrylic polymers.

Williams et al. disclose formulating halogenated xanthenes (photosensitizing agents) such as Rose Bengal with targeting moieties (penetrating solvents) in the form

Art Unit: 1641

of a gel, lotion, cream, ointment which have hydrophilic or hydrophobic moieties to enhance targeting of the agent into affected tissue and to improve effectiveness of sensitization of the target tissue. The targeting moieties may include chelators, complexing agents, long/short hydrocarbons (xerogels, polyacrylic polymers (see column 5, line 6 to column 6, line 29)).

It would have been obvious to one of ordinary skill in the art at the time of the invention to incorporate targeting moieties such as taught by Williams into halogenated xanthenes such as 4,5,6,7-tetrabromoerythrosin as taught by Heitz because Williams specifically taught that targeting moieties enhance targeting of the radiosensitizing agents into desired tissue to thus, improve effectiveness of sensitization of the target tissue. One of ordinary skill in the art at the time of the instant invention would have been motivated to incorporate targeting moieties such as taught by Williams into radiosensitizing agents such as taught by Heitz in order to prevent problems such as failure of radiosensitizing agents to adhere to desired tissue properly and consequent reduction of effectiveness of treatment by sensitization as a result thereof.

Response to Arguments

9. Applicant's arguments filed January 9, 2006 have been fully considered but they are not persuasive.

A) Applicant argues that Heitz et al. does not anticipate the claimed invention because the formulation of 4,5,6,7-Tetrabromoerythrosin is a novel composition of matter and a non-obvious extension of the halogenated xanthene class of molecules.

Art Unit: 1641

According to Applicant, there is no specific mention of 4,5,6,7-Tetrabromoerythrosin, and that the halogenated xanthenes as taught by Heitz make it clear that the disclosure pertains to pesticidal use as feed and not for intracorporeal use; and is not used to treat a disease in animal at all but rather prevents transmission of pathogens from one infected animal to another animal. Applicant specifically contends that Heitz et al. fail to teach a radiosensitizer agent used with ionizing radiation; but is rather used with optical energy such as visible light which is far below the recited independent claims. Applicant specifically argues that its use as a contrast agent is novel and nonobvious.

In response, Applicant's argument is not persuasive because Heitz et al. describe formulations of fluorescein derivatives having one or more substituents in the 4, 5, 6, 7, 2', 4', 5', and 7' positions selected from the group consisting of F, Cl, Br, with xanthene dyes including erythrosin B, phloxin B, eosin, and Rose Bengal in column 4, lines 12-31 which well encompasses the 4,5,6,7- Tetrabromoerythrosin recited in the claimed invention. In as far as its use as a pesticidal agent as taught by Heitz rather than a radiosensitizer agent for intracorporeal use and contrasting agent as in the claimed invention, a recitation of the intended use of the claimed composition must result in a structural difference between the claimed invention and the prior art in order to patentably distinguish the claimed invention from the prior art. If the prior art structure is capable of performing the intended use, then it meets the claim. See *In re Casey*, 370 F.2d 576, 152 USPQ 235 (CCPA 1967) and *In re Otto*, 312 F.2d 937, 939, 136 USPQ 458, 459 (CCPA 1963).

Art Unit: 1641

With respect to the recitation of “activated using X-rays having an energy greater than 30 keV” in claim 10, “using radiosensitization or ionizing radiation, ... approximately greater than or equal to 1 keV and less than or equal to approximately 1000 MeV” in claims 51 and 52, “[interacting with ionizing radiation applied... which] comprises X-rays” in claim 56, and “X-rays have an energy between 30 kiloelectron volts and 1000 megaelectron volts” in claim 57, again, a recitation of the intended use of the claimed invention must result in a structural difference between the claimed invention and the prior art in order to patentably distinguish the claimed invention from the prior art. If the prior art structure is capable of performing the intended use, then it meets the claim. See *In re Casey*, 370 F.2d 576, 152 USPQ 235 (CCPA 1967) and *In re Otto*, 312 F.2d 937, 939, 136 USPQ 458, 459 (CCPA 1963).

With respect to halogenated xanthenes such as 4,5,6,7-tetrabromoerythrosin being an imaging contrast agent with high solubility in aqueous solution and preference to hydrophobic environment, the discovery of a new property of an otherwise known compound or product such as 4,5,6,7-tetrabromoerythrosin, discovered to characteristically exist as an imaging contrast agent with high degree of solubility in aqueous solution and preference to hydrophobic environment, and which is capable of enhancing efficacy of ionizing radiation applied to cancer or tumor in radiation therapy, does not render the product novel, unless otherwise, rendered novel or nonobvious from a modification or variation of its original structure, i.e. “derivatized 4,5,6,7-tetrabromoerythrosin by attachment to a biological targeting moiety”, that is structurally

Art Unit: 1641

different, novel, and nonobvious from all other commercially known halogenated xanthenes.

B) Applicant argues that the combination of Williams et al. with Heitz et al. does not render obvious the claimed invention because neither Heitz et al. nor Williams et al. describe 4,5,6,7-Tetrabromoerythrosin which is a highly halogenated xanthene for use as radiosensitizer agent. Applicant specifically contends that Williams et al. describes a method of dye-mediated photocoagulation based on intense illumination of treated tissue that is fundamentally unrelated to the present invention.

Applicant's argument is not persuasive because the teaching of Williams et al. was combined with the teaching of Heitz et al. for the teaching of formulating halogenated xanthenes with targeting moieties in the form of chelators, complexing agents, long/short hydrocarbons (xerogels, polyacrylic polymers) or penetrating solvents which have hydrophilic or hydrophobic moieties to enhance targeting of the agent into affected tissue and to improve effectiveness of sensitization of the target tissue. Accordingly, It would have been obvious to one of ordinary skill in the art at the time of the invention to incorporate targeting moieties such as taught by Williams into the halogenated xanthenes encompassed by Heitz because Williams taught that targeting moieties enhance targeting of the radiosensitizing agents into desired tissue to thus, improve effectiveness of sensitization of the target tissue.

Allowable Subject Matter

Art Unit: 1641

10. Claim 68 is allowed. Prior art of record fails to teach or fairly suggest a radiosensitizer agent comprising a halogenated xanthene that is specifically attached to a biological targeting moiety to enhance targeting of the halogenated xanthene to desired cancer or tumor tissue.

11. Claim 14 is objected to as being dependent from a rejected base claim.

Correspondence

12. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Gailene R. Gabel whose telephone number is (571) 272-0820. The examiner can normally be reached on Monday, Tuesday, and Thursday, 7:00 AM to 4:30 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Long V. Le can be reached on (571) 272-0823. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Art Unit: 1641

Gailene R. Gabel
Patent Examiner
Art Unit 1641
March 31, 2006

A handwritten signature in black ink, appearing to read "G. Gabel", written diagonally across the typed name.